CASE REPORTS

- *Methemoglobinemia Simulating Bulbar Poliomyelitis*
- *Hypertrophic Pulmonary Osteoarthropathy*

Methemoglobinemia Simulating Bulbar Poliomyelitis

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A NINE-YEAR-OLD white boy was admitted to the Los Angeles County Hospital January 14, 1951. Several hours earlier he had lost consciousness at school and three physicians who examined him had concurred in a diagnosis of bulbar poliomyelitis.

Two weeks previously the patient had had fever, nausea, vomiting, and diarrhea which lasted four days. Upon physical examination the patient was noted to be acutely ill. The skin was pale and gray. There was pronounced hypoventilation and stupor. The patient vomited yellowish lumpy material which was casually referred to as "eggs" by one observer.

Oxygen under positive pressure was given while tracheotomy was started. The cut tissues and blood were brown, resembling chocolate milk, which suggested the diagnosis of methemoglobinemia. The laboratory reported a methemoglobin concentration of 66 per cent before treatment was instituted. Five milliliters of 1 per cent methylene blue in 45 ml. of normal saline solution was given intravenously. Within an hour the patient was talking, the color of the skin was normal, and the methemoglobin concentration was 22 per cent. The patient then said that he had eaten yellow crayons. (A tooth-marked piece of crayon had been found in a pocket of his garments.) Several hours later the patient was transferred to a private hospital, apparently well except for the tracheotomy incision.

On chemical analysis, the piece of crayon was reported to contain dyes of a group which includes benzidine yellow, vulcan fast yellow, ceylon yellow, and toner yellow. The exact type was not reported because of analytical difficulties on the small quantity of specimen.

Methemoglobin consists partially of iron which has been oxidized from the ferrous to the ferric form that does not transport oxygen. The process is slowly spontaneously reversible and does not damage the red cell. The symptoms result from generalized anoxia.

Treatment consists of the administration of reducing substances. Ascorbic acid acts too slowly and hence is not used in the acute form of the disease. Methylene blue intravenously in doses of 1 to 2 mg. per kg. of body weight given over a five-minute period is safe and effective. Methylene blue acts by speeding the reconversion mechanism of the normal cell.

Primary methemoglobinemia is rare and is due to a congenital biochemical defect in the erythrocytes. Secondary methemoglobinemia is usually due to drugs, of which nitrites, sulfonamides, and aniline derivatives are probably the most important. Phenacetin and acetanilid have frequently caused methemoglobinemia owing to their widespread use. Most cases of poisoning due to the ingestion of wax crayons have resulted from orange or yellow crayons. Flinn and co-workers reported that the feeding of wax crayons to animals did not produce methemoglobinemia. They concluded that since relatively few cases of poisoning in humans are reported, considering the frequency of wax crayon ingestion, the occasional poisoning with the material probably can be classed as an idiosyncrasy.

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Hypertrophic Pulmonary Osteoarthropathy

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THE AUTHORS recently observed a case of hypertrophic pulmonary osteoarthropathy in which the patient was first observed because of massive edema of the legs and the edema was dramatically relieved upon correction of the primary visceral disease.

Hypertrophic pulmonary osteoarthropathy, Marie's disease, was first described independently and almost simultaneously by Pierre Marie and von Bamberger in 1890. Since then, numerous reports have confirmed Marie's original description of the condition as symmetrical periostitis of the four extremities, involving mainly the phalanges and terminal epiphyses of the long bones of the forearm and leg. These changes sometimes involve the bones of the entire limb, and may be associated with dorsal kyphosis and some involvement of the joints, resulting in swelling of soft tissue and tenderness over the involved areas. Subperiosteal calcification may be observed in roentgen studies. The pathologic features are proliferative periostitis with subperiosteal new bone formation.

In the commonly observed simple clubbing of the fingers and toes, the involvement is one of soft tissue proliferation over the terminal phalanges. Osseous change is unusual. When osseous changes of atrophy and absorption of the terminal phalanges do occur, they are a late manifestation. By definition, in hypertrophic pulmonary osteoarthropathy

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skeletal changes are invariable.[7] However, whether simple clubbing is an early stage of hypertrophic pulmonary osteoarthropathy or a separate entity is not decided. Witherspoon[11] concluded that the prevailing evidence supports the former hypothesis. Weens and Brown[10] stated that in cases of clubbing in which there was bony absorption of the terminal phalanges, the absorption was preceded by hypertrophic changes. They presented reports of two cases to illustrate the point. Temple and Jaspin,[8] however, observed no such changes. They believed that no bony changes occur in simple clubbing of the fingers, and pointed out that changes such as those described can be normal variants. Cases of Marie's disease (as in the present instance) in which clubbing of the fingers and toes was not present have been reported.[7] It is generally believed that clubbing can occur as a separate entity or as an integral part of Marie's disease. Pattison and co-workers[7] stated that the fact that osseous change is not a constant finding in simple clubbing differentiates it from hypertrophic pulmonary osteoarthropathy, in which there is always osseous change.

Hypertrophic pulmonary osteoarthropathy is most frequently secondary to disease of the thoracic and abdominal viscera. However, it has been described in other conditions, including thyroid disease[9] and chronic myelogenous leukemia.[8] The primary disease is most commonly pulmonary and may be either neoplastic or infectious in character. However, the syndrome is also associated with cardiac, hepatic and gastrointestinal diseases, such as subacute bacterial endocarditis, congenital heart disease, cirrhosis, non-tropical sprue[8] and mediastinal tumors. A similar syndrome may occur as a manifestation of primary idiopathic disease (chronic idiopathic hypertrophic osteoarthropathy;[1] idiopathic familial osteophytosis[4]) predominantly in males at puberty and without associated visceral disease. This entity is felt to be familial[4] and is quite rare.

The clinical manifestations of hypertrophic pulmonary osteoarthropathy include pain and tenderness of the bones and joints and hypertrophy and edema of the soft tissue overlying involved bone. The onset is usually insidious, but in rare instances may be rapid.[6]

Often, as in the case presented here, the involvement of the extremities is the first clue to the diagnosis. This is more often true in neoplastic conditions than in those of inflammatory nature, where the primary disease is usually evident long before the onset of hypertrophic osteoarthropathy.[7]

Craig[3] diagnosed Marie's disease in three cases previously diagnosed as rheumatoid arthritis and in one diagnosed as acromegaly. (Marie's original description was written to clarify acromegaly and to define conditions which may be confused with it.[5])

Pattison and co-workers[7] pointed out the dramatic regression of symptoms and the swift objective improvement following removal of the primary lesion either surgically or by x-ray therapy. Within a matter of hours, the pain and swelling usually subside. Follow-up radiologic studies over a long period have not been carried out in many cases, and whether the roentgenologically observable changes regress or persist will require further study and observation.

The pathogenesis of hypertrophic pulmonary osteoarthropathy remains a mystery.[11, 8, 7] Endocrine,[5] vascular[2] and chemical[4] factors have been investigated without yielding an answer. Some change in the peripheral blood flow and consequent alteration in oxygenation of tissues seems to be the most likely explanation at present.[2]

The condition may be present without producing symptoms or signs. Therefore, it would probably be noted more frequently if detailed x-ray studies of the extremities were done in all patients with carcinoma of the lung.[8] The value of recognizing this condition, however, lies in the occasional case in which it leads to the early diagnosis and treatment of pulmonary neoplasm.

REPORT OF A CASE

A white man 65 years of age noted swelling of both legs up to the knees ten days before admittance to the hospital. For three days the swelling had been so severe and the pain so intense that the patient had been bedridden at home. The patient had smoked two packages of cigarettes daily for about 40 years. For the past 20 years he had a "cigarette cough," which was productive of small amounts of yellowish mucus when he awakened in the morning. For the preceding year the patient had noted nocturnal wheezing that was relieved by sitting up and by using a proprietary gargle, after which sleep was undisturbed. No loss of weight had occurred. There were no other symptoms referable to the lungs.

The patient was well developed, appeared to be well nourished and in no distress. The blood pressure was 120 mm. of mercury systolic and 75 mm. diastolic, the temperature 98.6° F., the pulse rate was 90 per minute, and respiration 24 per minute. Both legs were greatly swollen from the knees down, with a firm, pitting edema. The skin over this area seemed somewhat warmer than elsewhere, and there was definite tenderness of the ankles and over the shafts of the tibiae. There was no tenderness or thickening of the veins of the legs. Homan's sign was not present and no venous collateral circulation was evident. There was no clubbing of the fingers or toes.

Both hands seemed large and wide, but the patient stated that they had always been so. There was no tenderness or edema of the upper extremities.

Wheezes and a few crepitant rales were heard over the upper lobe of the left lung.

The circulation time, arm to tongue, with 10 per cent magnesium sulfate, was 20 seconds; arm to lung, with ether, it was 6 seconds. The venous pressure was 9 cm. of water. The hemoglobin content was 11 gm. per 100 cc. of blood. Leukocytes numbered 10,500 per cu. mm.—80 per cent filamented polymorphonuclear leukocytes, 6 per cent non-filamented polymorphonuclear leukocytes, 2 per cent eosinophilic leukocytes and 12 per cent lymphocytes. Results of the urinalysis were normal. The serum albumin content was 4.1 gm., and the serum globulin 3.2 gm. per 100 cc. The non-protein nitrogen content of the blood was 31 mg. per 100 cc. Sputum was negative for tubercle bacilli on three examinations. The vital capacity was 2,200 cc. Stool specimens were negative for occult blood. The femoral arterial blood oxygen saturation was 74 per cent and the femoral venous blood oxygen saturation was 68 per cent. The patient's hands, suspended in water, displaced 550 cc.

In x-ray films of the chest a mass in the hilum of the left lung and segmental atelectasis of the superior anterior segment of the upper lobe consistent with bronchogenic carcinoma or pulmonary tuberculosis were noted. Studies were made of the sputum by the Papanicolaou technique on three occasions, and cells suspicious of malignant disease were noted twice and definitely malignant cells once. In bronchoscopic examination the corina of the upper lobe of the left lung was observed to be congested and thickened, with a copious secretion coming from the bronchus of the upper lobe. A biopsy specimen and material for a smear were taken. Malignant cells were noted in the smear, and non-specific inflammation in the biopsy specimen. In x-ray

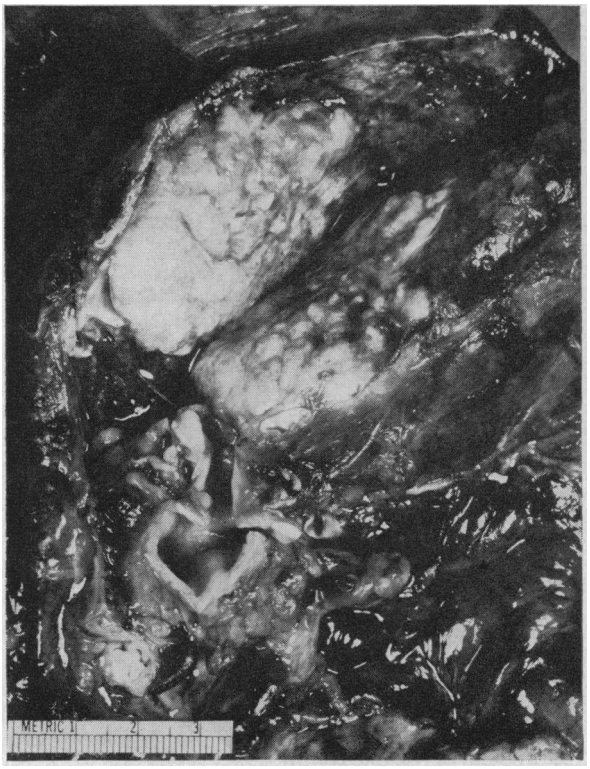

Figure 1.—Pathological specimen, left lung.

films of the extremities, subperiosteal new bone formation was noted in the tibiae, fibulae and distal ends of the femora.

The patient was treated with penicillin and aminophyllin and prophylactically with quinidine (to prevent arrhythmia) prior to thoracotomy. A bronchiogenic carcinoma involving the entire upper lobe of the left lung and invading the lower lobe and the hilum was observed at operation. Left pneumonectomy was done but it was impossible to remove all the involved tissue from the mediastinum. Upon pathological examination the upper lobe of the lung was noted to be enlarged and firm. On the cut surface of the upper lobe there was an area of firm, gray-white, homogeneous tissue, not too well circumscribed and about 5 cm. in diameter (Figure 1). Microscopically, large sheets of pleomorphic cells with pyknotic nuclei and many mitotic figures were noted. Much inflammation and necrosis were present. Malignant cells were present in the bronchial lumen. The pathological diagnosis was bronchogenic carcinoma.

The swelling and tenderness of the legs subsided completely the first postoperative day (Figure 2). The hands displaced 450 cc. of water. The patient stated that his legs and hands were of normal size and that, with retrospection, he recognized that his hands had been swollen. Subperiosteal calcification was noted in x-ray films ten days and one month after operation. A month postoperatively there was no recurrence of symptoms and the patient felt well.

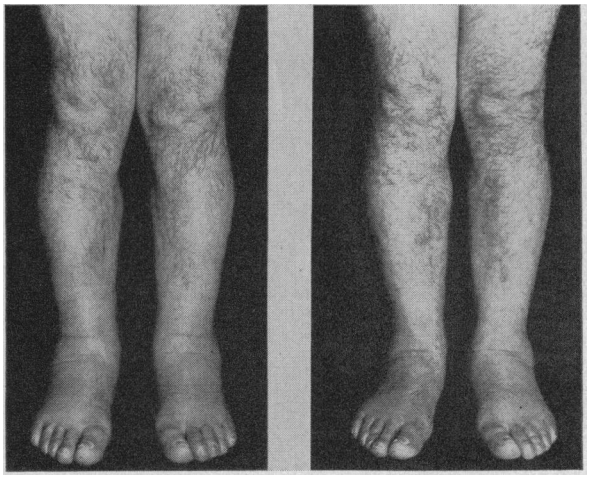

Figure 2.—*Left*, preoperative; *right*, postoperative.

SUMMARY

A case of bronchogenic carcinoma is presented, in which the presenting symptoms were due to hypertrophic pulmonary osteoarthropathy. Following pneumonectomy there was complete regression of the soft tissue swelling, without evidence of any change in the skeletal manifestations. In cases of swelling and pain of the extremities of obscure origin, this entity should be considered and a search made for visceral, especially pulmonary, disease.

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